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EXAMINER	
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ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/720,037	RASPE ET AL.	
	Examiner	Art Unit	
	SHULAMITH H. SHAFER	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *4-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 9-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20 March 2001*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, And/Or Claims:

Restriction Requirement:

Applicants' election, with traverse of Group I, claims 1-3 and 9-13, drawn to a method of screening for a substance useful in the treatment of a lipid metabolism dysfunction comprising contacting said substance with a Rev-erb receptor, in the reply filed on 26 June 2008 6 is acknowledged. The grounds for the traversal are:

a. In a generic Markush claim as presented in claim 1, separation of the claim into separate groups is improper

b. Office action has not demonstrated that an undue search burden would be required to examine all groups.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

Appendix B of the MPEP PCT-A1 states (with respect to "Markush Practice"):

"The situation involving the so-called "Markush practice" wherein a single claim defines alternatives (chemical or non-chemical) is also governed by Rule 13.2. In this special situation, the requirement of a technical interrelationship and the same or corresponding special technical features as defined in Rule 13.2, shall be considered to be met when the alternatives are of a similar nature.

(i) When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

(A) all alternatives have a common property or activity, and

(B) (1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives, or

(B) (2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

(ii) In paragraph (f)(i)(B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or

activity. The structural element may be a single component or a combination of individual components linked together.

(iii) In paragraph (f)(i)(B)(2), above, the words "recognized class of chemical compounds" mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved."

In response to traversal a: Claim 1 recites the following groups: (a) Rev-erb receptor; and (b) the response element of a Rev-erb receptor.

These groups do not have a common property or activity nor do they have a common structure. The Rev-erb receptor is a protein molecule which binds a ligand and can bind to the response element. The Rev-erb response element is a short sequence of DNA within the promoter region of a gene that binds the Rev-erb receptor complex and is therefore capable of regulating transcription. Thus, the members of the listed groups do not share a special technical feature and restriction is proper.

In response to traversal b: The instant application is a 35 U.S.C. § 371 filing, and MPEP § 1893.03(d), which describes restriction practice for applications filed under this statute states the following:

"Examiners are reminded that unity of invention (not restriction) practice is applicable in international applications (both Chapter I and II) and in national stage applications submitted under 35 U.S.C. § 371…When making a lack of unity of invention requirement, the examiner must (1) list the different groups of claims and (2) explain why each group lacks unity with each other group (i.e., why there is no single inventive concept) specifically describing the unique special technical feature in each group."

The Examiner is not required to demonstrate an undue search burden. The restriction requirement satisfied the requirements set forth in the MPEP.

On page 4 of Office Action of 18 of June 2008, a paragraph was included requiring an election of species. This paragraph was in error; no requirement for species election was made. The Examiner regrets any confusion arising from the error.

The restriction requirement is deemed proper and is therefore made FINAL.

Claims 1-13 are pending in the instant application. Claims 4-8 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a

nonelected invention, there being no allowable generic or linking claim. Claims 1-3, and 9-13 are under consideration to the extent they read on the elected invention which is summarized below.

Applicants' elected invention drawn to:

A method of screening for a substance which is useful in the treatment of a lipid metabolism dysfunction comprising contacting said substance with a Rev-erb receptor "and/or ...functional equivalent thereof." (independent claim 1), wherein the Rev-erb receptor is the hRev-erba receptor (Claim 2)

A process for screening a substance which is useful in the treatment of a lipid metabolism dysfunction comprising placing a test substance in contact with a receptor of the Rev-erb family or a functional equivalent thereof and measuring the binding of said test substance to the Rev-erb receptor (Independent claim 3)

A method for characterization or testing of the mechanism of action of a substance having anti-atherosclerotic properties comprising placing said substance in contact with a receptor of the Rev-erb family or a functional equivalent thereof and measuring the binding of said substance to the Rev-erb receptor (Independent claim 9).

Priority:

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in France on 25 June 1998. It is noted, however, that applicant has not filed a certified copy of the 1998 application (Fr 98/08093) as required by 35 U.S.C. 119(b), nor has a translated copy of the 1998 application been submitted. Therefore, benefit of the foreign priority filing dates is not granted. Priority is granted to the date of filing of PCT/EP99/04286, 21 June 1999.

Information Disclosure Statement:

The Information Disclosure statements (IDS) submitted on the 20 March 2001 has been considered. The signed copy is attached.

Objections

Specification:

37 CFR 1.74 (Reference to drawings) states:

> When there are drawings, there shall be a brief description of the several views of the drawings and the detailed description of the invention shall refer to the different views by specifying the numbers of the figures, and to the different parts by use of reference letters or numerals (preferably the latter). (MPEP § 608.01(f))

The specification is objected to because it does not contain a brief description of the drawings. The information presented in the drawings cannot therefore be evaluated.

Claims:

Claims 1-3, and 9-13 are objected to as reciting non-elected inventions. The claims should be amended to recite only the elected invention.

Claim 1 is objected to because of the following informalities: the claim is grammatically incorrect. It is suggested that “an Rev-erb receptor" should be amended to read “a Rev-erb receptor”.

Rejections

35 U.S.C. § 112, Second Paragraph:

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, and 9-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. While all of the technical details of a method need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is to be practiced. The omitted steps are: (a) a detection step measuring some effect which is a result of contacting the test substance with a Rev-erb receptor and (b) a correlation or conclusionary step describing how the results of the assay allow for the determination of a substance which is useful in treatment of lipid metabolism dysfunction.

Claim 3, an independent claim of the instant invention is an incomplete method claim. To be complete, a method claim must state a goal in the preamble of the claim, and conclude having achieved that goal. Claim 3 is directed to a method for screening a substance which is useful in the treatment of a lipid metabolism dysfunction. However, the method steps, as recited, are insufficient to accomplish the goal stated in the preamble. The method steps recite placing a test substance in contact with a receptor of the Rev-erb family and binding said test substance to the Rev-erb receptor. Thus, it is unclear if carrying out the method steps would result in accomplishing the goal set forth in the preamble. Claim 9 is vague and indefinite in reciting "A method for characterization or testing of the mechanism of action of a substance having anti-atherosclerotic properties comprising placing said substance in contact with the receptor of the Rev-erb family ….and measuring the binding of said substance to the Rev-erb receptor". The claim recites a binding assay. It is unclear how an assay the measures binding would characterize or test a mechanism of action of a test substance.

Furthermore, claim 9 is an incomplete method claim. To be complete, a method claim must state a goal in the preamble of the claim, and conclude having achieved that goal. Claim 9 is directed to a method for characterization or testing of the mechanism of action of a substance having anti-atherosclerotic properties. However, the method steps, as recited, are insufficient to accomplish the goal stated in the preamble. The method steps recite placing a test substance in contact with a receptor of the Rev-erb family and binding said test substance to the Rev-erb receptor. Thus, it is unclear if

carrying out the method steps would result in accomplishing the goal set forth in the preamble.

Claims 1, 3, and 9 are vague and indefinite in reciting "functional equivalent thereof". It is unclear what function the "functional equivalent" is to perform. Proteins have many functions, including stimulating antibody production, and serving as nutritional materials. Also, it is not clear to which of the named elements the "functional equivalent thereof" applies.

Claims 10 and 12 are vague and indefinite. It is unclear at which point in the method steps of claims 3 and 9, respectively, the expression level of apolipoprotein C-III is to be measured.

Claims 2, 11 and 13 are included in this rejection as dependent from a rejected claim.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 9-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a written description rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph.

The claims recite methods of screening or testing substances useful in the treatment of lipid metabolism dysfunction comprising contacting said test substance with a Rev-erb receptor or a functional equivalent thereof.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117). A review of the language of the claim indicates that these claims are drawn to a genus, i.e., methods comprising rev-erb receptors or functional equivalents thereof.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

There is a single species of the claimed genus disclosed that is within the scope of the claimed genus, *i.e.* the hRev-erbα receptor. However, the present claims encompasses numerous species that are not further described.

In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus, which is functional equivalents of the Rev-erb receptor. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus. The specification does not clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed (see *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3, and 9 are rejected under 35 U.S.C. 102(e) as being anticipated by Trueheart et al. (US 6,189,705, issued 12 December 2000, filed 24 September 1997, the '705 patent). The '705 patent teaches assays for screening and identifying pharmaceutically effective compounds that specifically interact with and modulate activity of a cellular receptor (abstract). The subject assays provide a means for detecting the ability of compounds to modulate the signal transduction activity of the target receptor by scoring for up or down regulation-regulation of a detection signal (column 2, lines 46-49). The tested compounds are exogenously added to cells comprising a heterologous receptor (column 3, lines 53-55) in order to identify potential effector compounds (column 3, lines 13-15). Thus, the reference teaches contacting a receptor with a test compound. One of ordinary skill in the art would recognize that modulating signal transduction activity of a receptor would require binding of the test compound to the cognate receptor; thus measuring changes in signal transduction activity would be a method of measuring or detecting binding of test compounds to the receptor. The heterologous receptor may be a human receptor (column 8, line 65). The '705 patent teaches that the target receptor of interest may be a nuclear receptors. The nuclear receptor may be one of the orphan nuclear receptors, including the Rev-erb receptor family (column 22, lines 37-59). The art teaches (See, for evidentiary purposes only, Vu-Dac et al. J Biol Chem. 1998. 273:25713-25720, page 25717, 2nd column, 2nd paragraph) the Rev-erb family of receptors comprises Rev-erbα (also know as EAR1), Rev-erbβ (also termed RVR and BD73) and E75. Thus, the '705 patent teaches screening compounds comprising contacting test substances with a Rev-erb receptor,

which may be a hRev-erbα receptor and measuring binding of said substance to the receptor and anticipates the limitations of claims 1-3 and 9.

35 U.S.C. § 103:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over the '705 patent as applied to claims 3 and 9 in view of Vu-Dac et al (1998. J Biol Chem. 273:25713-25720, page 25717) and further, in view of Fraser et al. (1997. J. Biol Chem. 1997. J Biol Chem. 272:13892-13898) and Auwerx et al. (1996. Atherosclerosis 124 Suppl:S29-S37). The teachings of the '705 patent are set forth in detail above. Additionally, the '705 patent teaches that identified test compounds identified by the described assay can be formulated in pharmaceutical preparations for in vivo administration to a human (column 56, lines 35'43). The '705 patent does not teach a method comprising the measuring the expression level of apolipoprotein C-III (apo C-III), wherein reduction in expression level of said apoC-III in the presence of said test

compound indicates that said test compound is useful in the treatment of a lipid metabolism dysfunction.

Vu-Dac et al teach that fibrates, which are hypolipidemic drugs, elevate mRNA levels of the nuclear receptor Rev-erbα. The resulting increase in Rev-erbα protein represses the transcription of Apolipoprotein A-1 (Apo-1) gene, thereby lowering cholesterol (abstract). Thus, the reference teaches that rev-erbα inhibits the transcription of Apo-1. The reference also teaches that fibrates have been shown to repress the transcription of a wide variety of genes involved in lipid and energy metabolism including the human, rat and mouse apoC-111 genes (page 29718, 2nd column, 2nd paragraph). Fraser et al. teach that apo-1 and apo-CIII genes are closely linked and appear to share regulatory elements (page 13892, 2nd column, 2nd paragraph). Auwerx et al teach that decreases in apo CIII protein concentration induces beneficial changes in lipoprotein profile and further teach that altering the expression of genes encoding for apolipoproteins constitutes an effective therapeutic option (page S35, section 5).

Thus, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of the '705 patent and measure changes in the expression level of apoC-III gene as a specific measure of signal transduction following binding of test compound to the rev-erbα receptor and identifying an agent that decreases the expression of Apo-CIII as a compound useful in treatment of a lipid metabolism dysfunction. The person of ordinary skill in the art would have been motivated to make these modifications and anticipate success because Vu-Dac et al. teach that Rev-erbα protein represses the transcription of Apolipoprotein A-1 (Apo-1) gene, Fraser et al. teach that apo-1 and apo-CIII genes appear to share regulatory elements and may thus be regulated by the same receptor protein, Auwerx et al teaches the therapeutic benefits of decreasing expression of genes encoding the Apo-CIII protein and the '705 patent teaches that test compounds identified by the screening assays taught in the reference are useful as therapeutic compounds.

Conclusion:

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHULAMITH H. SHAFER whose telephone number is (571)272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao, Ph.D. can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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